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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| Applicants: | Minoru Moriya et al. | Art Unit: 1625 |
| Serial No.: | 10/544,261 | Case No.: BY0006P |
| Filing Date: | January 17, 2006 | Examiner: Celia C. Chang |
| For: | MELANIN-CONCENTRATING HORMONE RECEPTOR ANTAGONISTS CONTAINING PIPERIDINE DERIVATIVES AS THE ACTIVE INGREDIENT | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT

Examiner:

This Amendment is in response to the Final Office Action dated August 3, 2009 and Advisory Action dated November 5, 2009, please enter the following amendments and remarks in the above-identified application. Submitted herewith is a Petition for Extension of Time for one month from November 3, 2009, to and including December 3, 2009.

No additional fee is believed to be due for this response. Should any fee be required, please charge such fee to Merck Deposit Account 13-2755.

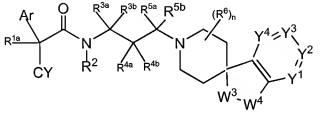
Amendments to the Claims begin on page **2** of this paper.
Remarks begin on page **9** of this paper.

IN THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-32. (Cancelled).

Claim 33. (Previously Presented) A compound of structural formula I-1:



[I-1]

or a pharmaceutically acceptable salt thereof,

wherein:

$R^{1a}$ is selected from: hydrogen, hydroxyl, and optionally halogen-substituted lower alkyl;

$R^2$ is optionally halogen-substituted lower alkyl;

$R^{3a}$, $R^{3b}$, $R^{5a}$ and $R^{5b}$ are each independently selected from: hydrogen and optionally halogen-substituted lower alkyl;

$R^{4a}$ and $R^{4b}$ are each independently selected from: hydrogen, halogen, hydroxyl, and optionally halogen-substituted lower alkyl;

each $R^6$ is independently selected from: hydrogen, halogen and optionally halogen-substituted lower alkyl;

n is selected from an integer between 1 and 8;

$W^3$ is –O–,

$W^4$ is $–CH_2–$,

CY is cyclopentane ring, cyclohexane ring, prrolidine ring, morpholine ring, piperazine ring, pyperidine ring, benzene ring, dihydropyridine ring, pyridine ring, pyrazine ring, pyrimidine ring, pyrrole ring, pyrazole ring, imidazole ring, triazole ring, tetrazole ring, oxazole ring, oxadiazole ring, oxazolidine ring and thiazole ring; which is optionally substituted with two or more substituents selected from Group α,

$Y^1$, $Y^2$, $Y^3$ and $Y^4$ are each independently selected from: –CH–, –CF–, $–C(NHCOCH_3)–$, $–C(NHCOC_2H_5)$ – and –N–,

with the proviso that not all of $Y^1$ to $Y^4$ are simultaneously nitrogen atoms;

Ar is a benzene ring, a pyridine ring, a pyrazine ring or a pyrimidine ring, unsubstituted or substituted with one or two substituents selected from Group β:

each Group α is independently selected from: halogen, hydroxyl, amino, nitro, oxo, mono-lower alkylamino, di-lower alkylamino, optionally halogen-substituted lower alkyl, optionally fluorine-substituted lower alkyloxy, lower cycloalkyloxy, lower alkyloxycabonyl, (lower alkyloxycarbonyl)amino, (lower alkyloxycarbonyl) lower alkylamino, lower alkylcarbonyl, lower alkylcarbonyloxy, (lower alkylcarbonyl)amino, (lower alkylcarbonyl) lower alkylamino, carbamoyl, mono-lower alkylcarbamoyl, di-lower alkylcarbamoyl, carbamoylamino, mono-lower alkylcarbamoylamino, di-lower alkylcarbamoylamino, (mono-lower alkylcarbamoyl) lower alkylamino, (di-lower alkylcarbamoyl) lower alkylamino, carbamoyloxy, mono-lower alkylcarbamoyloxy, di-lower alkylcarbamoyloxy, lower alkylsulfonyl, lower alkylsulfonylamino, sulfamoyl, mono-lower alkylsulfamoyl, di-lower alkylsulfamoyl, sulfamoylamino, (mono-lower alkylsulfamoyl)amino, (di-lower alkylsulfamoyl)amino, (mono-lower alkylsulfamoyl) lower alkylamino and (di-lower alkylsulfamoyl) lower alkylamino; and

each Group β is independently selected from: nitro, aryloxy, lower cycloalkyl, lower cycloalkyloxy, lower alkylenedioxy, halogen, hydroxyl, optionally hydroxyl- or fluorine-substituted lower alkyl and optionally fluorine-substituted lower alkyloxy.

Claim 34. (Previously Presented) The compound according to Claim 33, wherein $R^{1a}$ is hydrogen, methyl or hydroxyl; and pharmaceutically acceptable salts thereof.

Claim 35. (Cancelled).

Claim 36. (Previously Presented) The compound according to Claim 33, wherein both $R^{3a}$ and $R^{3b}$ are hydrogen atoms; and pharmaceutically acceptable salts thereof.

Claim 37. (Previously Presented) The compound according to Claim 33, wherein $R^{4a}$ and $R^{4b}$ are selected from the group consisting of hydrogen, fluorine and hydroxyl;
and pharmaceutically acceptable salts thereof.

Claim 38. (Previously Presented) The compound according to Claim 33, wherein $R^{5a}$ and $R^{5b}$ are hydrogen or methyl; and pharmaceutically acceptable salts thereof.

Claim ~~39~~. (Previously Presented) The compound according to Claim ~~33~~, wherein each $R^6$ is hydrogen; and pharmaceutically acceptable salts thereof.

Claims 40 and 41. (Cancelled).

Claim ~~42~~. (Previously Presented) The compound according to Claim ~~33~~, wherein CY is a substituent selected from the group consisting of phenyl, 4-fluorophenyl, 4-chlorophenyl, 3,4-difluorophenyl, 4-methoxyphenyl, 4-tolyl, 4-trifluoromethylphenyl, pyridinyl, pyridin-3-yl, pyrazinyl, pyrimidinyl, 6-fluoropyridin-3-yl, 2-fluoropyridin-4-yl, 6-trifluoromethylpyridin-3-yl, 6-methoxypyridin-3-yl, pyrrol-1-yl, pyrazolyl, imidazolyl, 2-methylimidazolyl, 4-methylimidazolyl, 1,2,3-triazol-1-yl, 4-methyl-1,2,3-triazol-1-yl, 1,2,4-triazol-1-yl, 1,2,3,4-tetrazol-1-yl, 1,2,3,4-tetrazol-2-yl, thiazolyl, pyrrolidin-1-yl, piperidinyl, 2-piperidon-1-yl, 2-pyridon-1-yl, 2-pyrrolidon-1-yl, oxazolidin-2-on-1-yl, 4-methanesulfonyl-piperazin-2-on-1-yl, cyclohexyl and cyclopentyl; or a pharmaceutically acceptable salt thereof.

Claim 43. (Cancelled).

Claim ~~44~~. (Previously Presented) The compound according to Claim ~~33~~, wherein Ar is a substituent selected from the group consisting of phenyl, 4-fluorophenyl, 3,4-difluorophenyl, 4-chlorophenyl, 4-methoxyphenyl, 4-tolyl, 4-trifluoromethylphenyl, pyridinyl, 6-fluoropyridin-3-yl, 6-trifluoromethylpyridin-3-yl, and 6-methoxypyridin-3-yl;
and pharmaceutically acceptable salts thereof.

Claim ~~45~~. (Currently Amended) The compound according to Claim ~~33~~ selected from the group consisting of:

(1) ~~2-(3,4-difluorophenyl)-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[5-fluoroisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,~~

~~(2)~~ 2-(3,4-difluorophenyl)-N-methyl-2-(1H-1,2,3-triazol-1-yl)-N- [3-(spiro [isobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(2)~~(3)~~ 2-(3,4-difluorophenyl)-N-methyl-2-(2H-1,2,3,4-tetrazol-2-yl)- N-[3-(spiro[isobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(3)~~(4)~~ 2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1(2H)pyridinyl)-N- [3-(spiro[isobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(4)~~(5)~~ 2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1- pyrrolidinyl)-N- [3-(spiro[5-fluoroisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]-acetamide,

(5)~~(6)~~ 2-(3,4-difluorophenyl)-N-methyl-2-(2-methyl-1H-imidazol-1- yl)-N-[3-(spiro[6-fluoroisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]-acetamide,

(6)~~(7)~~ 2-(3,4-difluorophenyl)-N-methyl-2-(2-methyl-1H-imidazol-1- yl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide,

(7)~~(8)~~ 2,2-bis(6-fluoro-3-pyridinyl)-N-methyl-N-[3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H),4'- piperidin]-1-yl)propyl]acetamide,

(8)~~(9)~~ 2-(3,4-difluorophenyl)-N-ethyl-2-(2-oxo-1-pyrrolidinyl)-N- [3-(spiro[isobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide,

(9)~~(10)~~ 2-(3,4-difluorophenyl)-N-ethyl-2-(4-methanesulfonyl)-2-oxo- 1-piperazinyl)-N-[3-(spiro[6-fluoroisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide, and
or a pharmaceutically acceptable salt thereof.

Claims 46-52. (Cancelled).

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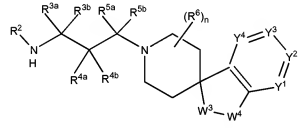
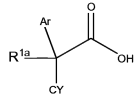
Claim 53. (Previously Presented) A method for producing a compound according to Claim 33 of general formula [I-1], which comprises:

(1) amidating a compound represented by a general formula [IIa]:



[IIa]

wherein $R^2$, $R^{3a}$, $R^{3b}$, $R^{4a}$, $R^{4b}$, $R^{5a}$, $R^{5b}$, $R^6$, $Y^1$, $Y^2$, $Y^3$, $Y^4$, $W^3$, $W^4$ and n are as in Claim 33, with a compound represented by a general formula [IIIa]



[IIIa]

wherein: Ar, $R^{1a}$ and CY are as in Claim 33.

Claims 54-57. (Cancelled).

Claim 58. (Previously Presented) The compound according to Claim 57 selected from the group consisting of:

(1) 2-(4-fluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N-[3- (spiro[6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(2) 2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N- [3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]- 1-yl)propyl]acetamide,

(3) 2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N- [3-(spiro[6-fluoro-5-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)- propyl]acetamide,

(4) 2-(3,4-difuorophenyl)-N-methyl-2-(2-methyl-1H-imidazol-1- yl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)- propyl]acetamide,

(5) 2-(3,4-difluorophenyl)-2,2-dimethyl-N-methyl-N-[3-(spiro[5- fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(6) 2-(3,4-difluorophenyl)-N-methyl-2-(1H-1,2,4-triazol-1-yl)-N- [3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(7) 2,2-bis(6-fluoro-3-pyridinyl)-N-methyl-N- [3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(8) N-methyl-2,2-bis(6-methoxy-3-pyridinyl)-N-[3-(spiro[5-fluoro- 6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(9) 2-(6-fluoro-3-pyridinyl)-2-(4-fluorophenyl)-N-methyl-N-[3- (spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(10) 2-(6-fluoro-3-pyridinyl)-N-methyl-2-(6-trifluoromethyl-3- pyridinyl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(11) 2-(6-fluoro-3-pyridinyl)-2-(6-methoxy-3-pyridinyl)-N-methyl- N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)- propyl]acetamide,

(12) 2-(6-fluoro-3-pyridinyl)-2-(4-toluyl)-N-methyl-N- [3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(13) 2-(6-fluoro-3-pyridinyl)-N-methyl-2-phenyl-N- [3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(14) 2,2-bis(4-fluorophenyl)-N-methyl-N-[3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(15) 2-(3,4-difluorophenyl)-N-methyl-2-(1H-pyrrol-1-yl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(16) 2-(4-fluorophenyl)-N-methyl-2-(1H-pyrrol-1-yl)-N-[3-(spiro[5- fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

(17) 2-(3,4-difluorophenyl)-N-methyl-2-(1H-pyrazol-1-yl)-N-[3- (spiro[5-fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]- acetamide,

(18) 2-(3,4-difluorophenyl)-N-methyl-2-(1H)-pyrrol-1-yl)-N-[3- (spiro[6-fluoro-5-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide,

(19) 2-(6-fluoro-3-pyridinyl)-2-(4-fluorophenyl)-N-methyl-N-[3 - (spiro[6-fluoro-5-azaisobenzofuran-1(3H),4-piperidin]-1-yl)propyl]- acetamide,

(20) 2-(6-fluoro-3-pyridinyl)-2-(4-fluorophenyl)-N-methyl-N-[3- (spiro[6-azaisobenzofuran-1(3H),4-piperidin]-1-yl)propyl]acetamide,

(21) 2,2-bis(6-fluoro-3-pyridinyl)-N-ethyl-N-[3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)-propyl]acetamide,

(22) 2-(6-fluoro-3-pyridinyl)-2-(2,4-difluorophenyl)-2-hydroxy-N- methyl-N-[3-(spiro[6-fluoro-5-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide,

(23) 2-(2,4-difluorophenyl)-2-(6-fluoro-3-pyridinyl)-2-hydroxy-N- methyl-N-[3-(spiro[6-azaisobenzofuran-1(3H), 4'-piperidin]- 1-yl)propyl]acetamide, or

(24) 2,2-bis(4-fluorophenyl)-2-hydroxy-N-methyl-N-[3-(spiro[5- fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide,

or a pharmaceutically acceptable salt thereof.

Claim 59. (Cancelled).